



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

December 22, 2015

SIEMENS HEALTHCARE DIAGNOSTICS, INC.
MATTHEW GEE
SENIOR MANAGER, REGULATORY AFFAIRS
511 BENEDICT AVENUE
TARRYTOWN NY 10591

Re: K142826

Trade/Device Name: ADVIA Centaur Toxoplasma M (Toxo M)
Regulation Number: 21 CFR 866.3780
Regulation Name: Toxoplasma gondii Serological Reagents
Regulatory Class: II
Product Code: LGD
Dated: December 3, 2015
Received: December 4, 2015

Dear Mr. Gee:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, “Misbranding by reference to premarket notification” (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH’s Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

 Ribhi Shawar -S

For Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

K142826

Device Name

ADVIA Centaur Toxoplasma M (Toxo M)

Indications for Use (Describe)

The ADVIA Centaur Toxoplasma M (Toxo M) assay is an IgM antibody capture microparticle direct chemiluminometric in vitro diagnostic immunoassay intended for the qualitative detection of IgM antibodies to Toxoplasma gondii in serum or plasma (EDTA, heparin) using the ADVIA Centaur and ADVIA Centaur XP systems.

The ADVIA Centaur Toxo M assay is used to measure IgM antibody against *T. gondii* which is presumptive of an acute, recent, or reactivated toxoplasma infection. Any measurement of IgM antibody to *T. gondii* must be performed in conjunction with the determination of IgG antibody to *T. gondii*.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRASstaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) Summary of Safety and Effectiveness

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of 21 CFR 807.92 and the Safe Medical Device Act of 1990.

The assigned 510(k) Number is: K142826

1. Date Prepared

April 9, 2015

2. Purpose for Submission

The purpose of this submission is to describe changes to the ADVIA Centaur Toxoplasma M (Toxo M) assay (K010755).

3. Measurand

Toxoplasma IgM antibodies

4. Type of Test

Immunoglobulin class-capture chemiluminescence immunoassay

5. Applicant Information

Contact: Matthew Gee, M.Sc.
Senior Manager, Regulatory Affairs

Address: Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591-5097

Phone: 914-524-2099

Fax: 914-524-3579

Email: matthew.gee@siemens.com

6. Proprietary and Established Names

ADVIA Centaur® Toxoplasma M (Toxo M)

7. Regulatory Information

Regulation Section: 21CFR 866.3780; Toxoplasma gondii Serological Reagents

Classification: Class II

Product Code: LGD

Device Classification Name: Enzyme linked immunoabsorbent assay, *Toxoplasma gondii*

Review Panel: Microbiology (83)

8. Predicate Device Information

Name: ADVIA Centaur Toxoplasma M (Toxo M)

Manufacturer: Siemens Healthcare Diagnostics Inc.

510(K) Number: K010755

510(k) Summary of Safety and Effectiveness

9. Intended Use

9.1 Intended Use

The ADVIA Centaur Toxoplasma M (Toxo M) assay is an IgM antibody capture microparticle direct chemiluminometric *in vitro* diagnostic immunoassay intended for the qualitative detection of IgM antibodies to *Toxoplasma gondii* in serum or plasma (EDTA, heparin) using the ADVIA Centaur and ADVIA Centaur XP systems.

The ADVIA Centaur Toxo M assay is used to measure IgM antibody against *T. gondii* which is presumptive of an acute, recent, or reactivated toxoplasma infection. Any measurement of IgM antibody to *T. gondii* must be performed in conjunction with the determination of IgG antibody to *T. gondii*.

9.2 Indications for Use

Same as Intended Use

9.3 Special Conditions for Use Statement(s)

The detection of toxoplasma IgM in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the toxoplasma IgM assay used. Values obtained with different assay methods cannot be used interchangeably. The reported IgM level cannot be correlated to an endpoint titer.

This assay is not intended for use in screening blood, plasma, or tissue donors. The effectiveness of this assay for use in screening blood, plasma, or tissue donors has not been established.

9.4 Special Instrument Requirements

ADvia Centaur and ADvia Centaur XP

10. Device Description

The ADvia Centaur Toxo M assay consists of the following:

Table 1. Summary of Ingredients of the ADvia Centaur Toxo M Assay Components

Component	Volume	Ingredients
ADvia Centaur Toxo M Lite Reagent	10.0 mL/pack	partially purified <i>T. gondii</i> antigen (~3 µg/mL) complexed with a mouse anti- <i>T. gondii</i> p30 monoclonal antibody (F(ab) ₂ fragment) labeled with acridinium ester in protein buffer with surfactant and preservatives
ADvia Centaur Toxo M Solid Phase	17.0 mL/pack	mouse anti-human IgM _µ monoclonal antibody (~24 µg/mL) covalently coupled to paramagnetic particles in protein buffer with surfactant and preservatives
ADvia Centaur Toxo M Calibrators	600 µL/vial	defibrinated recalcified processed human plasma positive for toxoplasma IgM antibodies with preservatives
ADvia Centaur Toxo M Controls	1.5 mL/vial	defibrinated recalcified processed human plasma negative and positive for toxoplasma IgM antibodies with preservatives

510(k) Summary of Safety and Effectiveness

11. Purpose of the Submission

The purpose of this submission is to submit a modification to the ADVIA Centaur Toxo M assay.

In addition to manufacturing process changes to improve operational effectiveness, and buffer changes to decrease the likelihood of non-specific binding, the main change to the ADVIA Centaur Toxo M assay is a truncation of the anti-p30 antibody in the Lite Reagent to remove the Fc portion of the molecule. This antibody is used to link the acridinium ester (chemiluminescent tag) to the toxoplasma p30 antigen. It is not involved in the binding of analyte from patient samples (i.e. not a component of reaction mechanism).

12. Comparison of Predicate Device and Modified Device

Table 3 provides a list the similarities of the currently marketed predicate ADVIA Centaur Toxo M assay (with a whole IgG antibody in the Lite Reagent) and the modified ADVIA Centaur Toxo M assay with a F(ab)₂ fragment in the Lite Reagent. Table 4 provides a list of differences between the predicate and modified devices.

Table 2. Similarities of Modified ADVIA Centaur Toxo M Assay and Predicate

Item	Predicate Device (K010755)	Modified Device
Intended Use	The ADVIA Centaur Toxoplasma M (Toxo M) assay is an IgM antibody capture microparticle direct chemiluminometric <i>in vitro</i> diagnostic immunoassay intended for the qualitative detection of IgM antibodies to <i>Toxoplasma gondii</i> in serum or plasma (EDTA, heparin) using the ADVIA Centaur and ADVIA Centaur XP systems. The ADVIA Centaur Toxo M assay is used to measure IgM antibody against <i>T. gondii</i> which is presumptive of an acute, recent, or reactivated toxoplasma infection. Any measurement of IgM antibody to <i>T. gondii</i> must be performed in conjunction with the determination of IgG antibody to <i>T. gondii</i> .	Same
Instrument Platforms	ADvia Centaur ADvia Centaur XP	Same
Methodology	Immunoglobulin class-capture sandwich immunoassay using direct, chemiluminometric technology	Same
Capture Antibody (Solid Phase)	Mouse anti-human IgM μ monoclonal antibody	Same
Tracer (Lite Reagent)	Toxoplasma p30 antigen bound to acridinium ester (via mouse anti- <i>T. gondii</i> p30 monoclonal antibody)	Same

510(k) Summary of Safety and Effectiveness

Table 2. Similarities of Modified ADVIA Centaur Toxo M Assay and Predicate

Item	Predicate Device (K010755)	Modified Device
Specimen Type	Serum or plasma (EDTA, heparin)	Same
Sample Volume	10 μ L	Same
Calibration	2-point calibration using Toxo M Cal	Same
Performance Characteristics	Positive Percent Agreement: 99.2% Negative Percent Agreement: 99.2%	Same

Table 3. Differences Between Modified ADVIA Centaur Toxo M Assay and Predicate

Item	Predicate Device (K010755)	Modified Device
Toxoplasma IgM Source (Calibrators, Controls)	Toxoplasma IgM positive human plasma pools	Cell culture supernatant of human anti-toxoplasma IgM monoclonal antibody-producing cells
Particle Resuspension	Particle resuspension with water	Particle resuspension with Wash 1 (phosphate buffered saline)
Lite Reagent Conjugate*	Ab format = Whole IgG Ab Concentration = 30 ng/mL Conjugate Loading Ratio = 30:1	Ab format = F(ab) ₂ fragment Ab Concentration = 12.5 ng/mL Conjugate Loading Ratio = 18:1
Solid Phase Buffer	Buffer: Tris (pH = 8.0) NaCl: 150 mM Surfactant: CHAPS = 0.1 g/L Blocker: Gelatin = 22.2 g/L Mouse IgG: 25 mg/L EDTA: none	Buffer: Tricine (pH = 8.0) NaCl: 300 mM Surfactant: Tween-20 = 2.2 g/L Blocker: sm-BSA = 10.0 g/L Mouse IgG: 100 mg/L EDTA: 0.7 g/L
Claimed Measuring Range[^]	0.10–40.00 Index	0.10–10.00 Index

* The modified antibody in the Lite Reagent recognizes same epitope as the antibody in the cleared device. It is simply used to attach the acridinium ester (chemiluminescent tag) to the toxoplasma p30 antigen. It is not part of the analyte-binding reaction mechanism.

13. Standard/Guidance Document References

The following recognized standards from Clinical Laboratory Standards Institute (CLSI) were used as a basis of the study procedures described in this submission:

- Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition (CLSI EP05-A2, 2004; Recognition No. 7-110)
- Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition (CLSI EP07-A2, 2005; Recognition No. 7-127)
- Stability testing of in vitro diagnostic reagents (European Committee for Standardization EN 13640:2002; Recognition No. 7-84)
- Medical devices – Application of risk management to medical devices (ANSI/AAMI/ISO 14971:2007/(R)2010; Recognition No. 5-70)

510(k) Summary of Safety and Effectiveness

14. Test Principle

The ADVIA Centaur Toxo M assay is an immunoglobulin class-capture sandwich immunoassay using direct, chemiluminometric technology. The anti-human IgM monoclonal antibody is covalently coupled to paramagnetic particles in the Solid Phase. In the Lite Reagent, the *T. gondii* antigen is complexed with an anti-p30 monoclonal antibody (F(ab)₂ fragment) labeled with acridinium ester. Antibody-antigen complexes will form if toxoplasma IgM is present in the sample.

ADvia Centaur systems automatically perform the following steps for the Toxo M assay:

- Dispenses 10 µL of sample into a cuvette.
- Dispenses 340 µL of Solid Phase and incubates the mixture for 18 minutes at 37°C.
- Separates the Solid Phase from the mixture and aspirates the unbound reagent.
- Washes the cuvette with Wash 1.
- Dispenses 200 µL Lite Reagent and incubates the mixture for 18 minutes at 37°C.
- Separates the Solid Phase from the mixture and aspirates the unbound reagent.
- Washes the cuvette with Wash 1.
- Dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.

A direct relationship exists between the amount of toxoplasma IgM activity present in the patient sample and the amount of relative light units (RLUs) detected by the system. A result of reactive (positive) or nonreactive (negative) is determined using an Index Value.

15. Performance Characteristics

Analytical performance (precision, interference with endogenous substances and potentially interfering agents) and testing with panel samples and patient samples was evaluated using the modified ADVIA Centaur Toxo M assay. The results were comparable to those established for the previous version of the device (currently-marketed predicate).

16. Conclusions

The results of performance testing and verification activities demonstrate that the design modifications to the ADVIA Centaur Toxo M assay do not impact its safety or effectiveness and do not alter its performance claims or alter its intended use, as described in the labeling.

Based on the results of comparative testing, the modified ADVIA Centaur Toxo M assay is substantially equivalent in principle and performance to the currently-marketed predicate device, ADVIA Centaur Toxo M, cleared under 510(k) K010755.